Catatonia in a 6-year-old Patient Following Disseminated Group A Streptococcus Infection

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ABSTRACT

Pediatric catatonia is a complex entity that is easily missed in the hospital setting and seldom reported in the literature. Here, we present the case of a 6-year-old previously healthy female patient who was initially thought to have intractable delirium secondary to disseminated Group A streptococcus (GAS) infection. Careful examination, utilization of the Pediatric Catatonia Rating Scale, and lorazepam challenge were key to elucidating the diagnosis. While GAS is most often associated with pediatric acute-onset neuropsychiatric syndrome (PANS) in the child and adolescent population, we reviewed the limited literature to suggest a mechanism by which it can lead to catatonia. Further systematic study of catatonia in the pediatric population is warranted to better understand pathogenesis and long-term neuropsychiatric outcomes.

KEYWORDS: Catatonia, pediatric catatonia, Group A streptococcus, neuropsychiatry

Catatonia is a neuropsychiatric syndrome characterized by diverse features including mutism, posturing, negativism, staring, rigidity, and echophenomenon.[1] There are unique challenges to identifying and diagnosing catatonia in the pediatric population, including under recognition in nonpsychiatric settings, which might lead to the current state of underdiagnosis for this cohort.[2] Fortunately, there is increasing recognition in the literature of this syndrome in the adolescent population and increased emphasis that all psychiatric providers be familiar with pediatric catatonia as a disease entity.[3] At the same time, there is scant literature on catatonia in young children, possibly because it is most readily recognized as a sequela of severe psychiatric illness,[2] which is less common at this age. Catatonia has been documented in children as young as 4 years of age,[4] which suggests that this diagnosis might be frequently missed due to lack of recognition and screening especially in the general hospital setting.

Numerous etiologies of catatonia have been identified, including psychiatric and primary medical causes. Infection, and more specifically immune dysregulation, has been implicated as a major medical cause of catatonia, possibly due to a direct neurotoxic effect that can be triggered by a multitude of viral, bacterial, or parasitic organisms.[5] Group A Streptococcus (GAS) infection in children has been highly studied as a cause of pediatric acute-onset neuropsychiatric syndrome (PANS), a condition notable for acute onset obsessive-compulsive disorder (OCD) or severe food intake restriction.[6] However, there have also been case reports implicating GAS infection in causing catatonia in adults.[5]

Here, we present the case of a young child seen by our pediatric psychiatry consultation-liaison service initially in the pediatric intensive care unit after concerns for intractable delirium were raised. A comprehensive history, careful physical exam, and lorazepam challenge were critical in distinguishing catatonia from delirium, and serial Pediatric Catatonia Rating Scale (PCRS) measurements were essential in ensuring improvement and resolution in this case.[7]

CASE VIGNETTE

The child was a 6-year-old female patient with no notable past medical or psychiatric history. Her development, including all milestones, was appropriate without any delays. Her presenting symptoms included high fever (105.2ºF) and vomiting, for which she was brought to the pediatrician and then the emergency department, but she was discharged home with a presumed viral illness. Two days later, the patient was taken to the emergency room again and subsequently admitted to a community hospital, but in decompensated septic shock. Laboratory studies were notable for a lactate of 20, leukocytosis of 31.7, transaminitis (AST 1914, ALT 472), as well as blood and wound cultures positive for GAS. She was admitted to the pediatric intensive care unit

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and required pressor medications. Her course was complicated by multi-organ failure, disseminated intravascular coagulation and limb ischemia with significant lower extremity abscesses. She was sedated, intubated, and paralyzed with fentanyl, midazolam, and vecuronium. Three days later, the patient was transferred to our institution due to the complicated nature of her case.

Following transfer, the patient was medically stabilized and vecuronium was discontinued to assess her mental status, which remained poor with limited ability to follow commands and no verbalization. A head computed tomography (CT) scan and magnetic resonance imaging (MRI) without contrast were performed, but they did not identify any significant abnormalities. Despite ongoing sedation, there were breakthrough periods of agitation that the primary team contributed to delirium, and treatment with risperidone 0.5mg every night/bedtime (QHS) was initiated. After approximately one week, the patient was extubated and transitioned to fentanyl PCA. Her risperidone dose was increased to 0.5mg twice a day (BID), due to episodes of agitation during the day that were presumed to be delirium. She required nasojejunal feeds to support necessary nutrition.

On Day 10, the patient developed left gaze preference and an acute change in mental status. She failed to respond to voice or pain and showed seizure-like movements. A stroke code was activated, and neurology was consulted out of concern for seizure versus stroke versus hypoactive delirium. Her MRI showed a hyperintensity of unclear significance concerning for thrombus versus low flow versus artifact. Environmental measures to combat delirium were implemented and dexmedetomidine was discontinued. Of note, on this day, the patient coincidentally received a wound dressing change and was pretreated with lorazepam 1mg intravenous (IV), which resulted in complete return to her baseline neurological status. The neurology consultation, which occurred after lorazepam administration, documented an unremarkable mental status and neurologic exam, except for unexplained left gaze preference. A subsequent electroencephalogram (EEG) showed diffuse slowing, a nonspecific indicator of diffuse cerebral dysfunction, as seen in delirium, metabolic derangement, toxicity, and other types of diffuse encephalopathy. No seizure activity was captured. Her waxing-waning symptoms were again attributed to delirium in the setting of critical illness. A bedtime dose of risperidone 0.75mg was added in addition to the 0.5mg BID doses.

The additional dosing of risperidone did not prove effective in improving the patient's altered mental status or symptoms of presumed delirium. Her functioning was well below baseline, and she had minimal verbal output and only intermittently followed commands. However, she did not have any evidence of abnormal movements or other symptoms concerning for an acute neurologic process. On Day 14, the patient had a wound debridement and dressing change under anesthesia using propofol. Immediately following the procedure, the patient's parents and primary medical team again noted her to be significantly more lucid and able to follow commands than she had been in days. A consult to psychiatry was officially placed for assistance with delirium management.

On Day 15, the psychiatry consult service met with the patient and her parents for consultation. Her parents mentioned that compared to her baseline, the patient had significantly decreased movement and spontaneous speech production and was sometimes completely unresponsive. Her parents also shared that the previous day, the patient had been much more lucid following her wound dressing change, with her mother noting "it was very strange, I thought she would be asleep after anesthesia, but she was the most awake she's been in weeks." On exam, the patient appeared as if attempting to speak but was inhibited for unknown reasons. She had poor attention testing but was able to track objects and blink on command, and she had increased tone in her upper extremities. The paradoxical reaction to sedating medications in conjunction with our physical exam findings led us to believe that she could be suffering from catatonia. A PCRS score of 13 was recorded: stupor (1), starting (2), rigidity (2), withdrawal (2), mutism (3), reduced PO intake (3).

The psychiatry consult service recommended a lorazepam challenge with 1mg IV lorazepam. Within approximately 45 minutes of administration, the patient's response was dramatic and rapid. Her parents felt as if their daughter had "suddenly come back," and the pediatric intensive care unit (PICU) team was astounded at her improvement. For the first time since admission, the patient began to speak, first in whispers and then in audible sentences. Her score on the pediatric catatonia scale after administration of Ativan dropped to 8: staring (1), rigidity (1), withdrawal (1), mutism (2), refusal to eat/drink (3). As her response was diagnostic for catatonia, and she was started on Ativan 1mg IV every six hours (q6h), and the risperidone was discontinued. The following day, a repeat PCRS showed a score of 3: rigidity (1), withdrawal (1), mutism (1). Her upper extremity tone improved but remained increased. Within four days on continuous IV lorazepam, the patient's PCRS was scored as 0; she was no longer rigid, and she continued to have improved mental status (per parents to about 80% of baseline—they reported she still more sedate and less talkative than baseline). A plan to taper the lorazepam was initiated, with a deliberately slow decrease over two weeks to minimize the risk of reemergence of catatonia. There was no reemergence of catatonia or delirium symptoms at any point during or after the taper. By approximately Day 10 of lorazepam treatment, parents reported she was at her baseline mental status.

The patient's hospitalization was complicated by bilateral below knee amputations and multiple digit amputations as a result of her GAS infection, and she was discharged to a rehabilitation hospital after nearly three months in the hospital. After the resolution of her catatonia, the child psychiatry consult team's role remained quite active, using medical play and behavioral interventions to address the psychological stress experienced by the patient. She did not meet criteria for any additional psychiatric diagnosis, including OCD or other neuropsychiatric symptoms, during the remainder of her hospitalization.

DISCUSSION

This case highlights the potential role of GAS infection in the genesis of symptoms of catatonia and illustrates the difficulties in making a diagnosis of catatonia in young children. The neurobiologic underpinnings of catatonia remain largely unknown, although alterations in GABAeric and gutamatergic neural activity, as well as hypoactivity in cortical motor areas of frontal and parietal

cortex, have been implicated.[8] There have been a number of single case reports that have identified a wide range of pediatric illnesses as triggering catatonic episodes, including epilepsy, encephalitis, Wilson disease, Prader-Willi syndrome, and fever of unknown origin.[9] A recent meta-analysis found that 1 in 5 cases of catatonia had a medical cause – and of these cases, the majority (29%) were attributed to CNS inflammation, while sepsis, as seen in this case, accounted for roughly two percent of cases.[10] This distinction might be somewhat arbitrary, as sepsis leads to microglial activation and subsequent proinflammatory mediators.[11]

GAS is a Gram positive, beta-hemolytic coccus in chains that can cause mild illnesses, such as acute pharyngitis or impetigo, or more serious illness, such as necrotizing fasciitis or toxic shock syndrome. GAS infection in children and adolescents has garnered special interest in psychiatry because of pediatric autoimmune neuropsychiatric disorders associated with streptococcal infections (PANDAS), whereby infection is thought to trigger acute-onset OCD via neural autoimmunity. Autoimmunity has been implicated as a casual mechanism of catatonia, perhaps most prominently in N-methyl-D-aspartate (NMDA) receptor encephalitis. Another potentially overlapping mechanism for catatonia includes infection, possibly via direct neurotoxic effect or from secondary immunological response.[5] Neuroinflammation, mediated by microglia in white matter tracts, has been implicated in underlying cause of catatonic signs in both mouse models and humans.[12] It is notable in the patient's case that there were no underlying psychiatric symptoms or psychiatric symptoms that appeared following lysis of her catatonia. In this case, the patient responded immediately to benzodiazepine treatment; were this not the case, further immunologic work-up would have been warranted. Ferrafiat and colleagues propose that all children and adolescents with catatonia be given a thorough work-up for autoimmune causes, and a high dose corticosteroid test be considered.[13]

Although there appears to be increasing recognition of the importance of identifying and treating catatonia in adolescents,[3,14] the literature on catatonia in children in particular remains sparse. One review article identified 73 cases of pediatric catatonia (the youngest patient was 8 years of age).[9] In reviewing the literature, we identified one additional case report of a 4-year-old child with catatonia (which involved a specific genetic mutation),[4] but otherwise no cases in children as young as this patient. We hypothesize that there might be many other cases of undiagnosed catatonia in young children; although comprehensive epidemiologic studies have not been conducted, estimates of catatonia in pediatric psychiatry outpatients are five percent, compared to about 30 percent for children hospitalized with schizophrenia.[15,16] Our conjecture is that medical causes of catatonia in young children are particularly likely to be missed without astute examination given the relatively rarity of this diagnosis and the overlap with symptoms of delirium.

This case demonstrated the importance of a broad differential diagnosis and careful physical and mental status examination when assessing children with altered mental status. At times, the clinical phenotypes of delirium and catatonia can be quite similar, as both disease processes are associated with notable deficits in communication and level of consciousness. Examining the PCRS reveals that many of the 20 items (including stupor, mutism, withdrawal, staring, and reduced oral intake) are not uncommonly seen in delirium, and in fact patients with medical catatonia typically meet criteria for delirium.[17] Making the correct diagnosis in the pediatric population is critical and requires nuanced understanding of their core diagnostic differences. One specific feature in this case was the family's recognition that the patient's symptoms improved markedly following the serendipitous administration of propofol, a $GABA_A$ agonist (not dissimilar from lorazepam), during wound debridement. Another was the patient's increased upper extremity rigidity, although it is difficult to say whether this was a result of relatively high-dose antipsychotic administration or a symptom of catatonia. The importance of making an accurate diagnosis of catatonia cannot be understated given the marked differences in treatment between delirium and catatonia. In this case, the initial treatment received by the patient, risperidone, could have worsened the patient's condition, as antipsychotic medication (especially higher potency) can potentially worsen catatonia and highlights the importance of an accurate diagnosis.[18] In our patient's case, no signs of malignant catatonia, a potentially fatal form of illness, which includes fever and autonomic instability, were present. There have been prior case reports of malignant catatonia in children,[19] where electroconvulsive therapy (ECT) might be indicated. Although it has been understudied, there is case report level evidence to suggest that ECT might be safe and effective in treating pediatric catatonia.[20]

There are no consensus guidelines for the diagnosis or treatment of catatonia in young children. In this case, we chose lorazepam 1mg IV for the 'lorazepam challenge' to make the diagnosis. This was based on a brief literature review, which revealed that 1 to 2mg was used in adolescent case studies and in consideration of other doses of sedating medication the patient had received.[21] Lorazepam was then titrated to effect, and slowly and cautiously tapered over time, in much the same way as is done for adult patients with catatonia. Our patient required a maximum total daily dose of 4mg of lorazepam. It is difficult to say how low or high this dose is given the few comparable cases in the literature. Of particular importance for this case was the reliance on the parents' report about how close the patient was to her baseline. At 6 years of age, differences in temperament and milestone achievement might obscure otherwise routine examination techniques, for example, the patient at her baseline did not typically know the date, but she could always readily rapidly identify any character in her favorite movie, Frozen.

Pediatric catatonia is a complex diagnostic entity that can be mistaken for other entities such as delirium, and it is critical that psychiatrists be prepared to diagnose and treat catatonia not just in adults or the psychiatrically ill population. While the mechanism of catatonia is still being elucidated, dysregulation of the immune system. In this case, triggered by GAS infection is one potential mechanism. Systematic study of pediatric catatonia would be an important next step as a number of questions – including incidence/prevalence, disease pathophysiology, optimal treatment strategy, and long-term outcomes remain unresolved.

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